

**REMARKS**

**I. THE ELECTION/RESTRICTION REQUIREMENT**

Applicants acknowledge herein the finality of the election/restriction requirement. Applicants ask that the Office reconsider the election requirement in that it is clear that the nucleic acid sequences and their corresponding amino acid sequences clearly share a common technical feature. Applicants reserve the right to petition the Commissioner and/or file divisional applications on the non-elected claims.

**II. THE OBJECTION TO CLAIM 20**

The Office Action objects to claim 20 for lacking a terminal period. In response, the amendment to claim 20 obviates any basis for the objection. Reconsideration and withdrawal of the objection are respectfully requested.

**III. THE REJECTION UNDER 35 U.S.C. § 101**

The Office Action rejects claim 10 under 35 U.S.C. § 101, asserting that the claim does not distinguish the claimed yeast or fungus from a product of nature. In response, the amendment to claim 10 obviates any basis for the rejection. Reconsideration and withdrawal of this aspect of the rejection are respectfully requested.

The Office Action rejects claims 1, 10, 17-22, 25-28 and 49-53 under 35 U.S.C. § 101, asserting that the claimed invention is not supported by a specific, substantial and credible utility or a well established utility. In particular, the Office Action asserts that the specification merely discloses that SEQ ID NO: 285 is upregulated by a factor of 0.17 as a result of Bax-induced cell death and that no other information is provided. Applicants respectfully traverse the rejection.

The PTO has the initial burden of challenging a presumptively correct assertion of utility in the disclosure. Only after the PTO provides evidence showing that one of ordinary skill in the art would reasonably doubt the asserted utility does the burden shift to the applicant to provide rebuttal evidence sufficient to convince the person of the invention's asserted utility. In re Brana, 51 F.3d 1560 (Fed. Cir. 1995).

The claimed invention is directed to a specified isolated nucleic acid molecule wherein the expression of the specified isolated nucleic acid molecule is varied by a factor of 5 or more as a result of Bax-induced cell death. From the Office's use of the 0.17 value

(which on its face is not 5 or more), it appears that the Office misunderstood the data provided in the specification. The specification discloses that the specified isolated nucleic acid molecule has been identified as one whose expression is modulated upon programmed cell death. See, e.g., Abstract. The specification discloses that the specified isolated nucleic acid can be employed as a selective target for drugs to treat infections caused by or associated with yeast and fungi or for the treatment of proliferative disorders or for the prevention of apoptosis in certain diseases. See Abstract.

The specification discloses that Applicants identified a range of specific nucleotide sequences which are involved in the molecular pathways eventually leading to programmed cell death. As explained in Example 2, genes showing a difference of a factor of 5 or more in expression as a result of Bax-induced cell death, were identified as differentially expressed candidate genes. Page 3, lines 10-16. These sequences and their homologues in other yeast and fungi as well as the polypeptides which they encode represent novel molecular targets which can be incorporated into an assay to selectively identify compounds capable of inhibiting or activating expression of such polypeptides. Furthermore, the invention also relates to the potential use of said sequences in alleviating disease. Page 8, lines 20-30. The list in Table 1 includes all genes for which mRNA levels changed more than five fold in a first experiment (see Example 2). Page 5, lines 1-5. The factor by which the transcript level was affected, is expressed as the Qt value. A Qt value higher than 1 indicates upregulation while a Qt value lower than 1 indicates a downregulation. For instance, a Qt of 0.5 indicates a two-fold lower transcript level of a particular mRNA due to Bax expression in *S. cerevisiae*. Upregulation or downregulation of a specific mRNA is stated when Qt had a value of at least 5 or at most 0.21, respectively. Page 5, lines 6-11. The specification further discloses that it has been found that expression of the mammalian Bax gene triggers cell death in *Saccharomyces cerevisiae* and the fission yeast *Schizosaccharomyces pombe* with morphological changes similar to apoptosis. Page 2, lines 13-16. This can be an indication that the molecular pathways eventually leading to programmed cell death may also be partially present in yeast cells and other unicellular eukaryotes. Page 2, lines 18-20.

Underexpression or overexpression of any component of a process (e.g. translation) could lead to altered sensitivity to an inhibitor of a relevant step in that process. (See Sandbaken et al., 1990; Hinnebusch and Liebman 1991; Ribogene PCT WO 95/11969, 1995).

Such an inhibitor should be more potent against a cell limited by a deficiency in the macromolecule catalyzing that step and/or less potent macromolecules, as compared to the wild type (WT) cell. Page 33, lines 18-24. The component which is present in altered form or amount in a cell whose growth is affected by a test compound is potentially the site of action of the test compound. Page 33, lines 32-35. Thus, the claimed invention meets the utility requirement of 35 U.S.C. § 101. Reconsideration and withdrawal of the rejection of claims 1, 10, 17-22, 25-28 and 49-53 under 35 U.S.C. § 101 are respectfully requested.

**IV. THE REJECTION UNDER 35 U.S.C. § 112, FIRST PARAGRAPH**

The Office Action rejects claims 1, 10, 17-22, 25-28 and 49-53 under 35 U.S.C. § 112, first paragraph, asserting that (1) one skilled in the art would not know how to use the claimed invention; (2) the claimed invention contains subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the art that Applicants had possession of the claimed invention. Applicants respectfully traverse the rejection.

Applicants respectfully submit that for the reasons provided in response to the rejection of claims 1, 10, 17-22, 25-28 and 49-53, (1) one skilled in the art would know how to use the isolated nucleic acid molecule and corresponding amino acid sequence claimed in claims 1, 10, 17-22, 25-28 and 49-52; and (2) the claimed invention is described in the invention so as to convey to one skilled in the art that Applicants had possession of the claimed invention. Reconsideration and withdrawal of the rejection of claims 1, 10, 17-22, 25-28 and 49-53 under 35 U.S.C. § 112, first paragraph, are respectfully requested.

**V. THE REJECTION UNDER 35 U.S.C. § 112, SECOND PARAGRAPH**

The Office Action rejects claims 1, 10, 17-22, 25-28 and 49-53 under 35 U.S.C. § 112, second paragraph, asserting that the claims are indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

Applicants respectfully submit that for the reasons provided in response to the rejection of claims 1, 10, 17-22, 25-28 and 49-53, the claims are definite in that they particularly point out and distinctly claim that which Applicants regard as the invention. Reconsideration and withdrawal of the rejection of claims 1, 10, 17-22, 25-28 and 49-53 under 35 U.S.C. § 112, second paragraph, are respectfully requested.

**CONCLUSION**

Early consideration and prompt allowance of the pending claims are respectfully requested. Should the Office require anything further it is invited to contact Applicants' representative at the telephone number listed below.

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